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## Global proteomic analyses of human cytotrophoblast differentiation/invasion.

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### Public Summary:

During human pregnancy, cytotrophoblasts (CTBs) from the placenta differentiate into specialized subpopulations that play crucial roles in proper fetal growth and development. A subset of these CTBs differentiate along an invasive pathway, penetrating the decidua and anchoring the placenta to the uterus. A crucial hurdle in pregnancy is the ability of these cells to migrate, invade and remodel spiral arteries, ensuring adequate blood flow to nourish the developing fetus. Although advances continue in describing the molecular features regulating the differentiation of these cells, assessment of their global proteomic changes at mid-gestation remain undefined. Here, using sequential window acquisition of all theoretical fragment-ion spectra (SWATH), which is a data-independent acquisition strategy, we characterized the protein repertoire of second trimester human CTBs during their differentiation towards an invasive phenotype. This mass spectrometry-based approach allowed identification of 3026 proteins across four culture time points corresponding to sequential stages of differentiation, confirming the expression dynamics of established molecules and offering new information into other pathways involved. The availability of a SWATH CTB global spectral library serves as a beneficial resource for hypothesis generation and as a foundation for further understanding CTB differentiation dynamics.

### Scientific Abstract:

During human pregnancy, cytotrophoblasts (CTBs) from the placenta differentiate into specialized subpopulations that play crucial roles in proper fetal growth and development. A subset of these CTBs differentiate along an invasive pathway, penetrating the decidua and anchoring the placenta to the uterus. A crucial hurdle in pregnancy is the ability of these cells to migrate, invade and remodel spiral arteries, ensuring adequate blood flow to nourish the developing fetus. Although advances continue in describing the molecular features regulating the differentiation of these cells, assessment of their global proteomic changes at mid-gestation remain undefined. Here, using sequential window acquisition of all theoretical fragment-ion spectra (SWATH), which is a data-independent acquisition strategy, we characterized the protein repertoire of second trimester human CTBs during their differentiation towards an invasive phenotype. This mass spectrometry-based approach allowed identification of 3026 proteins across four culture time points corresponding to sequential stages of differentiation, confirming the expression dynamics of established molecules and offering new information into other pathways involved. The availability of a SWATH CTB global spectral library serves as a beneficial resource for hypothesis generation and as a foundation for further understanding CTB differentiation dynamics.

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